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PAPER

A practicable environmentally benign one-pot synthesis of 2-arylbenzofurans at room temperature†

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An environmentallyfriendly one-pot synthesis of 2-arylbenzofurans under ambient temperature has been developed. It features an *ortho*-hydroxyl group assisted Wittig reaction of substituted salicylaldehyde followed by an *in situ* oxidative cyclization. Its advantages include readily available and non-hazardous materials, benign reaction conditions (room temperature, green solvent and one-pot manner), easy work-up and high overall yields. Utilizing this methodology, various 2-aryl-benzofurans including four natural products have been synthesized.

Introduction

The benzofuran motif is widely presented in natural products and biologically active compounds.[1] It has drawn extensive attention due to its broad range of biological activities with significant pharmaceutical potentials in anticancer,[2] antiviral,[3] antifungal,[4] and immunosuppressive,[5] *etc*. To date, various methodologies have been developed to prepare benzofuran-containing analogs, including: (a) metal-mediated Sonogashira couplings,[6] C–C[7] or C–O[8] arylation reactions and oxidative aromatic C–O bond formation;[9] (b) oxidative cyclization of *o*-vinylphenols;[10] (c) dehydration of α-phenoxy ketones;[11] (d) intramolecular McMurry couplings[12] or Wittig reactions.[13] Generally, the application of these reported methodologies has been limited by several factors: (a) unavailable starting materials; (b) relatively harsh reaction conditions; (c) expensive transition-metal catalysts; and (d) multiple steps and low yields.

Previously we have reported a two-step synthesis of benzofurans. It involved a selective cross-McMurry coupling of the substituted salicylaldehyde with an aromatic aldehyde, followed by the oxidative cyclization.[14] One major challenge of this synthetic protocol is the difficult separation of the *ortho*-vinylphenols from the by-products produced during the cross-McMurry couplings. Therefore, it is highly desirable to develop a convenient and eco-friendly synthesis of the *ortho*-vinylphenols. We believed that this could be achieved through the Wittig reaction of a readily available substituted salicylaldehyde with triphenylphosphonium. Although a number of reports have discussed improving the green credentials of Wittig reactions using a solventless procedure[15] or using aqueous media,[16] the Wittig reactions of salicylaldehyde or protected salicylaldehyde were usually carried out using either strong bases such as *n*-BuLi,[17] $(Me_3Si)_2NNa$,[10d] *t*-BuOK[18] or other organic bases such as DBN,[19] along with the relatively harsh conditions.

Herein we report an environmentally friendly Wittig reaction of substituted salicylaldehyde without protecting groups. The reaction was achieved in high yield at room temperature using KOH in an environmentally benign solvent (PEG-600). Utilizing this greener Witttig reaction, a facile one-pot synthesis of 2-arylbenzofurans has also been developed.

Results and discussion

Our initial studies started with the Wittig reaction of salicylaldehyde (**1a**) with benzylphosphonium chloride (**2a**) in the presence of several readily available inorganic bases. As shown in Table 1, Na_2CO_3, K_2CO_3, K_3PO_4, LiOH, and NaOH could promote the reaction to some extent at room temperature (Table 1, entries 1–5). Here the best results were obtained when using KOH as a base (Table 1, entries 6–9), while the solvent effect indicated that better results were obtained with the non-polar solvent, such as toluene or hexane (Table 1, entries 10–14).

It is usually considered that at least two equivalents of base are needed to promote the Wittig reaction of the unprotected salicylaldehyde, one for neutralizing OH and one to deprotonate the triphenylphosphonium.[17,18] Nevertheless, our experiments demonstrated that this Wittig reaction could proceed in high yield using only 1.2 equivalents of KOH (Table 1, entries 8 and 14). We rationalized that the hydroxyl group of the salicylaldehyde could play a role that assists the Wittig reaction, as illustrated in Scheme 1. In contrast to the general impression that protecting groups are usually required for any acidic protons (OH, NH, *etc.*) on either ylide or carbonyl components, in this case the corresponding Wittig reaction can be conducted under milder conditions than those without the *ortho*-hydroxyl group.

This rationale has been further confirmed by the fact that the reaction of the potassium salt of salicylaldehyde with benzylphosphonium chloride also afforded the corresponding alkene in

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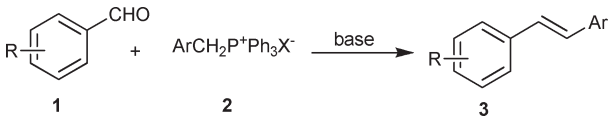
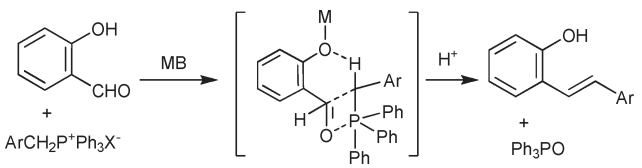
† Electronic supplementary information (ESI) available: Characterization data for known benzofurans and NMR spectra for all compounds. See DOI: 10.1039/c2gc16181h

Table 1 Effect of solvents, bases and hydroxyl group on the Wittig reaction at ambient temperature[a]



Entry	Aldehyde	Phosphonium salt	Base	Solvent	Yield[b] (%)
1	**1a** (R = *o*-OH)	**2a** (Ar = Ph; X = Cl)	Na_2CO_3 (2.0 eq.)	$PhCH_3$	44
2	**1a**	**2a**	K_2CO_3 (2.0 eq.)	$PhCH_3$	45
3	**1a**	**2a**	K_3PO_4 (2.0 eq.)	$PhCH_3$	67
4	**1a**	**2a**	$LiOH{\cdot}H_2O$ (2.0 eq.)	$PhCH_3$	58
5	**1a**	**2a**	NaOH (2.0 eq.)	$PhCH_3$	79
6	**1a**	**2a**	KOH (2.0 eq.)	$PhCH_3$	89
7	**1a**	**2a**	KOH (1.5 eq.)	$PhCH_3$	89
8	**1a**	**2a**	KOH (1.2 eq.)	$PhCH_3$	89
9	**1a**	**2a**	KOH (1.1 eq.)	$PhCH_3$	85
10	**1a**	**2a**	KOH (1.2 eq.)	EtOH	45
11	**1a**	**2a**	KOH (1.2 eq.)	DMF	45
12	**1a**	**2a**	KOH (1.2 eq.)	CH_3CN	58
13	**1a**	**2a**	KOH (1.2 eq.)	CH_2Cl_2	68
14	**1a**	**2a**	KOH (1.2 eq.)	hexane	86
15	**1b** (R = *o*-OK)	**2a**	—	$PhCH_3$	88
16	**1c** (R = *o*-OMe)	**2a**	KOH (1.2 eq.)	$PhCH_3$	78[c]
17	**1d** (R = *m*-OH)	**2a**	KOH (1.2 eq.)	$PhCH_3$	NR[d]
18	**1e** (R = *p*-OH)	**2a**	KOH (1.2 eq.)	$PhCH_3$	NR[d]
19	**1f** (R = H)	**2b** (Ar = *o*-HOC_6H_4; X = Br)	KOH (1.2 eq.)	$PhCH_3$	NR[d]
20	**1f**	**2c** (Ar = *m*-HOC_6H_4; X =Cl)	KOH (1.2 eq.)	$PhCH_3$	NR[d]

[a] The mole ratio of aldehyde (**1**) to phosphonium salt (**2**) was 1 : 1.1. [b] Isolated yield. [c] Only 10–20% conversion was observed after overnight stirring at ambient temperature, and the yield was obtained after heating at reflux for 8 h. [d] No reaction (NR) was observed after overnight stirring at ambient temperature or at reflux (above 8 h).



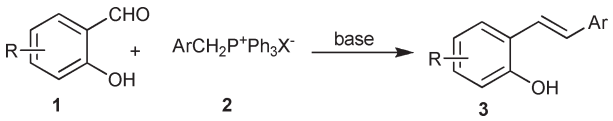
Scheme 1 *ortho*-Hydroxyl group assisted Wittig reaction.

high yield (88%) (Table 1, entry 15). In contrast, the Wittig reaction of 2-MeOPhCHO with benzylphosphonium chloride went slowly at room temperature and only afforded the desired product after heating at reflux for 8 h (Table 1, entry 16). No products were observed for the reactions of 3- or 4-hydroxybenzaldehyde with benzylphosphonium chloride (Table 1, entries 17 and 18) or PhCHO with 2- or 3-hydroxybenzylphosphonium bromide (Table 1, entries 19 and 20), even after the reaction mixtures were stirred at reflux temperature for 8 h. These experimental data correlated well with our proposed mechanism.

Overall, compared with the reported procedures,[17,18] the aforementioned Wittig reaction of salicylaldehyde can be carried out under significantly milder conditions (*e.g.* with only 1.2 eq. of KOH at room temperature). Since organic solvents are usually one of largest contributors to the magnitude of the Wittig reaction E factor,[20] in order to improve the green credentials of this Wittig reaction, we attempted to conduct the reaction in a solvent-free manner or in an eco-friendly solvent. In the solvent-free case, the neat reaction mixture was pulverized with a pestle and mortar at ambient temperature. Repeated tests indicated that the reactions in solid phase went very slowly at room temperature and yields were inconsistent. The best yield obtained was 53% (Table 2, entry 1). Similarly the results from using aqueous media were not ideal either (Table 2, entries 2 and 3). Next, given the fact that polyethylene glycol (PEG) has been proven to be a green solvent[21] and has been widely used in biotechnology and medicine,[22] we tested the Wittig reaction in this benign solvent. Among the PEGs screened, the reaction in PEG-600 gave a better result with a shorter reaction time and in higher yield at room temperature (Table 2, entries 4–7). Meanwhile, it was found that the recovered PEG-600 can be re-used several times (up to five times) without losing its activity (Table 2, entry 7). This condition was also applied to the other substrates (Table 2, entries 9–13), and as expected, the corresponding *o*-vinylphenols were obtained in high yields as well. It was noted that the ester group was tolerable even if KOH was used in the reactions (Table 2, entry 10).

We also carried out the Wittig reaction on a larger scale (10 mmol of **1a**, 11 mmol of **2a**, 12 mmol of KOH, 50 mL of PEG-600), the yield was almost identical to that obtained in the small scale (~86%). This demonstrated the potential of a large scale application for this protocol. Additionally, the post-Wittig reaction did not involve any organic solvent. After the reaction time, the mixture was directly poured into water and acidified with aqueous HCl solution. The resulting precipitate was collected and the filtrate was concentrated to recover the PEG-600. The crude products were subjected to further purification either through recrystallization (Table 2, entries 6, 10, 11) or by flash column chromatography. The newly formed triphenylphosphine oxide was also collected in high yield, which can be reduced back to triphenylphosphine if needed.[23]

Table 2 Wittig reactions of the unprotected salicylaldehyde in the solid phase or in an eco-friendly solvent[a]



Entry	Aldehyde	Phosphonium salt	Solvent	Conditions	Yield[b] (%)
1	**1a**	**2a**	—	RT, 12 h	53
2	**1a**	**2a**	H_2O	RT, 20 h	34
3	**1a**	**2a**	H_2O	80 °C, 16 h	63
4	**1a**	**2a**	PEG-300	RT, 38 h	76
5	**1a**	**2a**	PEG-400	RT, 36 h	75
6	**1a**	**2a**	PEG-600	RT, 12 h	86(73)[c]
7	**1a**	**2a**	PEG-600[d]	RT, 12 h	85[e],83[f]
8	**1a**	**2a**	PEG-800	RT, 48 h	82
9	**1b**	**2a**	PEG-600	RT, 17 h	86
10	**1a**	**2d** (Ar = 4-MeOOCC$_6$H$_4$; X = Cl)	PEG-600	RT, 12 h	89(76)[c]
11	**1a**	**2e** (Ar = 4-MeOC$_6$H$_4$; X = Cl)	PEG-600	RT, 16 h	85(71)[c]
12	**1g** (R = 3-OMe)	**2a**	PEG-600	RT, 14 h	87
13	**1g**	**2e**	PEG-600	RT, 16 h	86

[a] The mole ratio of aldehyde (**1**), phosphonium salt (**2**) and KOH was 1 : 1.1 : 1.2. [b] Isolated yield. [c] Yields in parenthesis were obtained after purification based on recrystallization. [d] Recovered PEG-600. [e] Yield was obtained when recovered PEG-600 was used for up to three times. [f] Yield was obtained when recovered PEG-600 was used for 4–5 times.

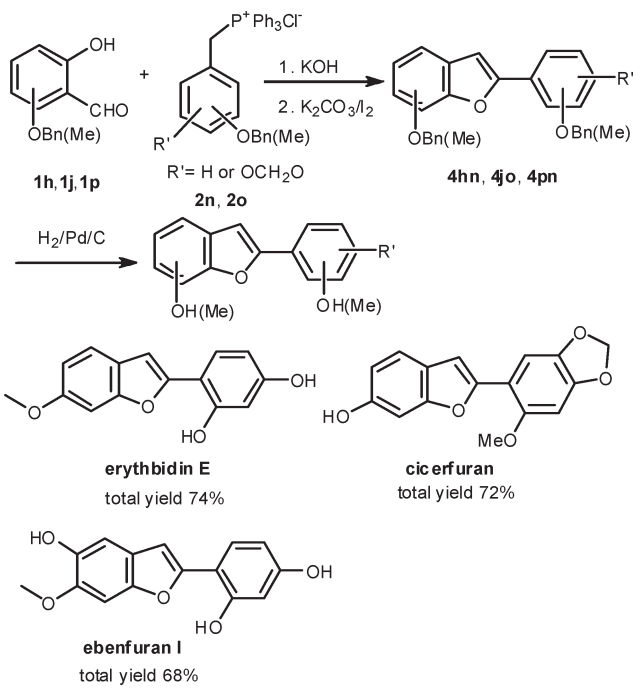
Utilizing this Wittig reaction, we further developed the one-pot synthesis of 2-arylbenzofuran in an eco-friendly manner. This was achieved through the Wittig reaction of substituted salicylaldehyde with triphenylphosphonium, followed by *in situ* oxidative cyclization of the resulting *o*-vinylphenols. Here I_2/K_2CO_3[10a,14] was chosen for the oxidative cycliztion because iodine is an inexpensive, non-toxic, readily available reagent. The generality and flexibility of this approach has been well established (Table 3). Corresponding Wittig reactions proceeded smoothly in most cases, and electron-donating groups, such as MeO– was beneficial to the oxidative cyclization of *o*-vinylphenols, leading to higher overall reaction yields. Corresponding work-up was very straightforward and similar to the Wittig reaction.

This one-pot synthetic approach offers one of the most practicable, effective and environmentally benign protocols for the preparation of 2-arylbenzofurans. Its advantages include: readily available and non-hazardous materials, benign reaction conditions (room temperature, green solvent and one-pot manner), easy work-up and high overall yields. In addition, this approach does not require the use of transition metal catalysts. Because it is very challenging to prepare halogen (especially iodine)-incorporated benzofurans through metal-mediated Sonogashira couplings,[6] C–C[7] or C–O[8] arylation reactions, our current protocol should address this limitation to readily yield the halogen-containing benzofurans (Table 3 entries 13–17).

Finally we applied this protocol to the synthesis of several naturally occurring benzofuran compounds. Corsifuran C,[24] isolated from *Corsinia coriandrina* as an origin of stilbenoid, was made using the one-pot reaction providing the desired product in 91% yield (Table 3, entry 9). Erythbidin E,[25] cicerfuran[10d,14a] and ebenfuran I[26] were readily prepared in only two steps, starting from the Wittig reactions of benzyloxy-substituted salicylaldehydes (**1h–1p**) with benzylphosphonium chlorides (**2n**and**2o**), followed by the deprotection step (illustrated in Scheme 2).

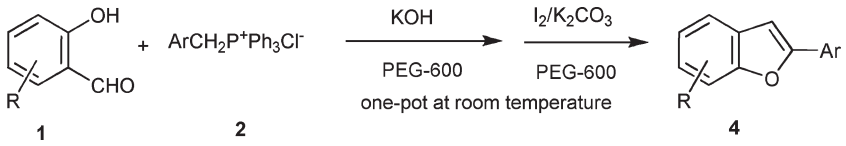
Conclusions

We have developed an environmentally friendly Wittig reaction of the substituted salicylaldehyde without any protecting groups. The reaction proceeded *via* an *ortho*-hydroxyl-assisted mechanism. Its advantages include: the use of a green solvent at room temperature, easy work-up and high yields. Based on this green Wittig reaction, a one-pot synthesis of 2-arylbenzofurans has also been developed in an eco-friendly manner. The one-pot synthetic approach features readily available and non-hazardous



Scheme 2 Total synthesis of cicerfuran, ebenfuran I and erythbidin E.

Table 3 One-pot synthesis of 2-arylbenzofuran at ambient temperature in PEG-600



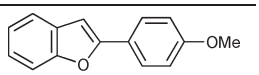
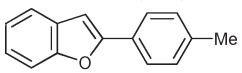
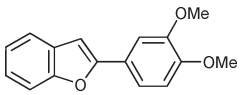
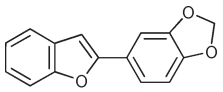
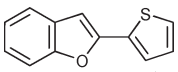
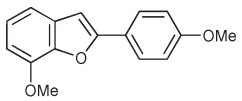
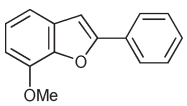
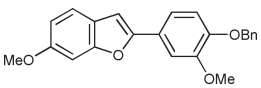
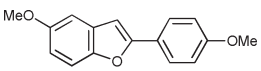
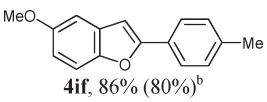
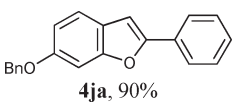
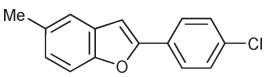
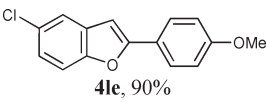
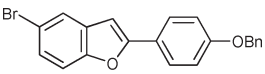
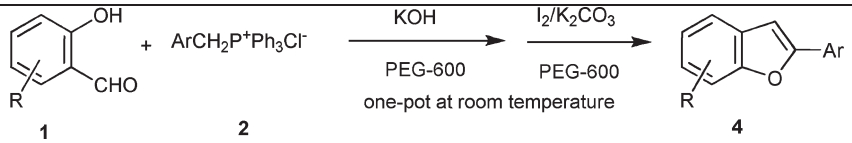
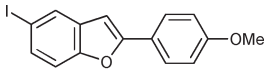
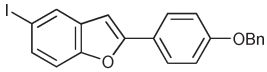
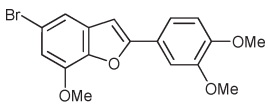
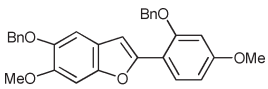
Entry	Aldehyde	Phosphonium salt	Product (yield)[a]
1	**1a**	**2e**	 **4ae**, 81% (74%)[b]
2	**1a**	**2f** (Ar = 4-MeC_6H_4)	 **4af**, 80% (71%)[b]
3	**1a**	**2g** (Ar = 3,4-$(MeO)_2C_6H_3$)	 **4ag**, 83% (73%)[b]
4	**1a**	**2h** (Ar = 3,4-$(OCH_2O)C_6H_3$)	 **4ah**, 86%
5	**1a**	**2i** (Ar = thiophen-2-yl)	 **4ai**, 78% (70%)[b]
6	**1g**	**2e**	 **4ge**, 88%
7	**1g**	**2a**	 **4ga**, 68%
8	**1h** (R = 4-MeO)	**2j** (Ar = 3-MeO-4-$OBnC_6H_3$)	 **4hj**, 82%
9	**1i** (R = 5-MeO)	**2e**	 **4ie** (Corsifuran C), 89%
10	**1i**	**2f**	 **4if**, 86% (80%)[b]
11	**1j** (R = 4-BnO)	**2a**	 **4ja**, 90%
12	**1k** (R = 5-Me)	**2k** (Ar = 4-ClC_6H_4	 **4kk**, 80%
13	**1l** (R = 5-Cl)	**2e**	 **4le**, 90%
14	**1m** (R= 5-Br)	**2l** (Ar = 4-$BnOC_6H_4$)	 **4ml**,77%

Table 3 *(Contd.)*



Entry	Aldehyde	Phosphonium salt	Product (yield)[a]
15	**1n** (R = 5-I)	**2e**	 **4ne**,88% (78%)[b]
16	**1n**	**2l**	 **2nl**, 78%
17	**1o** (R = 5-Br-3-MeO)	**2g**	 **4og**, 75%
18	**1p** (R = 4-MeO-5-OBn)	**2m** (Ar = 2-BnO-4-MeC$_6$H$_3$)	 **4pm**, 65%

[a] Overall isolated yield. [b] The yields were obtained after further purification either by flash column chromatography or through recrystallization (in parenthesis).

materials, benign reaction conditions (room temperature, green solvent and one-pot manner), easy work-up and high overall yields. Following this methodology, various 2-arylbenzofurans including four natural products have been readily synthesized.

Experimental

All reagents required for this study were purchased from commercial sources. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Bruker Avance DPX 400 (400 MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. MS were recorded on a TRACE mass spectrometer. IR spectra were recorded on a Vaatar 360 FT-IR spectrometer. Melting points are uncorrected.

General procedure for the Wittig reaction of (substituted) salicylaldehyde in PEG-600

To 10 mL of PEG-600, salicylaldehyde (**1**, 2.0 mmol), benzyltriphenylphosphonium chloride or bromide (**2**, 2.2 mmol) and KOH (164 mg, 2.4 mmol) was added. The mixture was stirred at room temperature until the reaction was completed (monitored by TLC). The reaction mixture was poured into water (50 mL), acidified to pH 2–3 with a 2 N HCl aqueous solution, after which a (sticky) solid was formed (*Note*: when the solid was sticky, silica gel (~5 g) was added and stirred for 0.5 h). The mother liquor was filtered off and subjected to vacuum distillation to recover the PEG-600. The filtered solid was treated with light petroleum–ethyl acetate at reflux temperature. After it was cooled to room temperature, the precipitated triphenylphosphine oxide was obtained in over 90% yield, which should be reduced back to triphenylphosphine according to the reported method.[23] The filtrate was evaporated and the resulting residue was further purified by recrystallization or chromatography on silica gel column to give desired product **3**.

General procedure for the one-pot synthesis of the 2-arylbenzofurans

A mixture of salicylaldehyde (**1**, 1.0 mmol), benzyltriphenylphosphonium chloride (**2**, 1.1 mmol) and KOH (82 mg, 1.2 mmol) in PEG-600 (5 mL) was stirred at room temperature until the reaction was completed (monitored by TLC). The mixture was diluted with 5 mL of PEG-600, and finely ground anhydrous K_2CO_3 (1.1 g, 8.0 mmol) was added. The stirring was continued for 2–3 h before iodine (2.1 g, 8.0 mmol) was added. After the oxidative cyclization was complete (monitored by TLC), the mixture was poured into water (50 mL), and treated with saturated aqueous $NaHSO_3$ to remove the unreacted iodine. The obtained solid and mother liquor were dealt with in the same way as described in the general procedure for the Wittig reaction. The desired 2-arylbenzofurans **4** were obtained after the work-up described above.

Characterization data for unreported 2-arylbenzofurans

2-(4-(Benzyloxy)-3-methoxyphenyl)-6-methoxybenzofuran (4hj)

White solid; m.p. = 118–120 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (d, J = 7.4 Hz, 2H), 7.35–7.43 (m, 4H), 7.30–7.34 (m, 2H), 7.07 (d, J = 1.5 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 6.86 (dd, J_1 =

8.5 Hz, J_2 = 2.1 Hz, 1H), 6.83 (s, 1H), 5.21 (s, 2H), 4.0 (s, 3H), 3.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.7, 155.6, 155.1, 149.7, 148.2, 136.9, 128.6, 127.9, 127.2, 124.2, 122.7, 120.7, 117.3, 114.0, 111.7, 108.1, 99.9, 95.8, 70.9, 56.0, 55.7; MS (AP) *m*/*z* 361 $(M + H)^+$. Anal. calcd for $C_{23}H_{20}O_4$: C, 76.65; H, 5.59; Found: C, 76.53; H, 5.71.

2-(4-(Benzyloxy)phenyl)-5-bromobenzofuran (4ml)

White solid; m.p. = 197–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.8 Hz, 2H), 7.69 (s, 1H), 7.32–7.48 (m, 7H), 7.05 (d, J = 4.8 Hz, 2H), 6.83 (s, 1H), 5.13 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 157.3, 153.5, 136.6, 131.5, 128.7, 128.2, 127.5, 127.5, 126.6, 126.5, 123.2, 123.0, 115.9, 115.3, 99.1, 70.1; MS (EI) *m*/*z* 380 (M^+, 40%), 287 (35%), 179 (45%), 91 (100%); Anal. calcd for $C_{21}H_{15}BrO_2$: C, 66.51; H, 3.99; Found: C, 66.27; H, 3.98.

2-(4-(Benzyloxy)phenyl)-5-iodobenzofuran (4nl)

White solid; m.p. = 187.7–189.3 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 1.5 Hz, 1H), 7.70 (d, J = 8.8 Hz, 2H), 7.44 (dd, J_1 = 8.6 Hz, J_2 = 1.6 Hz, 1H), 7.31–7.40 (m, 4H), 7.27 (d, J = 7.1 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.8 Hz, 2H), 6.73 (s, 1H), 5.05(s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.1, 156.2, 153.3, 136.7, 132.1, 132.0, 129.0, 128.4, 127.7, 126.4, 121.9, 115.3, 113.3, 99.4, 99.3, 87.2, 69.3; MS (AP) *m*/*z* 427 $(M + H)^+$; Anal. calcd for $C_{21}H_{15}IO_2$: C, 59.17; H, 3.55; Found: C, 59.26; H, 3.78.

5-(Benzyloxy)-2-(2-(benzyloxy)-4-methoxyphenyl)-6-methoxy benzofuran (4pm)

White solid; m.p. = 157.1–158.5 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, J = 8.2 Hz, 1H), 7.31–7.51 (m, 10H), 7.10 (s, 1H), 7.04 (s, 1H), 6.99 (s, 1H), 6.61 (d, J = 7.8 Hz, 2H), 5.21 (s, 2H), 5.16 (s, 2H), 3.95 (s, 3H), 3.83 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.2, 156.2, 151.6, 148.8, 148.3, 145.3, 137.4, 136.5, 128.7, 128.5, 127.7, 127.6, 127.4, 121.8, 113.4, 105.7, 105.1, 104.6, 100.0, 95.4, 71.9, 70.5, 56.3, 55.4; MS (AP) *m*/*z* 467 $(M + H)^+$. Anal. Calc. for $C_{30}H_{26}O_5$: C, 77.24; H, 5.62; Found: C, 77.20; H, 5.71.

2-(2,4-Bis(benzyloxy)phenyl)-6-methoxybenzofuran (4hn)

White solid; m.p. = 130.5–132.1 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, J = 9.2 Hz, 1H), 7.26–7.44 (m, 11H), 7.02 (s, 1H), 6.97 (d, J = 1.4 Hz, 1H), 6.75 (dd, J_1 = 8.5 Hz, J_2 = 2.2 Hz, 1H), 6.62 (dd, J_1 = 5.6 Hz, J_2 = 2.2 Hz, 2H), 5.12 (s, 2H), 5.02 (s, 2H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.5, 157.6, 156.3, 154.6, 151.5, 136.6, 136.4, 128.7, 128.6, 128.2, 128.1, 127.7, 127.6, 127.5, 123.3, 120.8, 113.5, 106.1, 111.3, 106.1, 104.4, 100.8, 95.6, 70.5, 70.2, 55.7; MS (AP) *m*/*z* 437 [$(M + H)^+$, 100], 179 (34). Anal. Calc. for $C_{29}H_{24}O_4$: C, 79.80; H, 5.54; Found: C, 79.40; H, 5.44.

2-(2,4-Bis(benzyloxy)phenyl)-5-(benzyloxy)-6-methoxy-benzofuran (4pn)

White solid; m.p. = 157.1–158.5 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.92 (d, J = 9.3 Hz, 1H), 7.30–7.50 (m, 15H), 7.09 (s, 1H), 7.03 (s, 1H), 6.99 (s, 1H), 6.69–6.70 (m, 2H), 5.19 (s, 2H), 5.15 (s, 2H), 5.08 (s, 2H), 3.94 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.4, 156.2, 151.6, 148.9, 148.4, 145.3, 137.4, 136.6, 136.5, 128.7, 128.6, 128.4, 128.1, 127.7, 127.6, 127.5, 127.4, 121.8, 113.6, 106.1, 105.8, 104.7, 100.8, 95.4, 71.9, 70.5, 70.2, 56.3; MS (AP) *m*/*z* 543 $(M + H)^+$. Anal. Calc. for $C_{36}H_{30}O_5$: C, 79.68; H, 5.57; Found: C, 79.34; H, 5.80.

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